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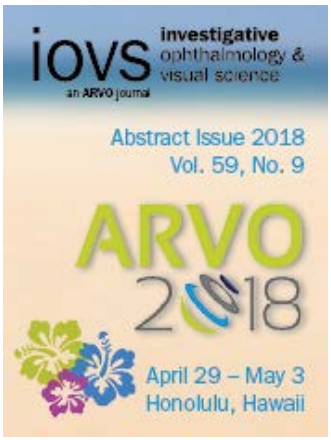

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Microfluidic platform to study pressure-induced changes in neurons

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Abstract

Purpose :Explore a model for glaucoma by developing methods to image *Caenorhabditis elegans* neuronal function in response to controlled pressure modulation

Methods :Microfluidic devices have been developed for imaging behavior and cellular processes in *C. elegans*. These devices are

fabricated using polydimethylsiloxane (PDMS), an inert polymer. External pressure is adjusted to immobilize the animal as well as to control flow of solutions in the devices (Figure 1a). Here we developed and tested modified versions of microfluidic devices (Hulme et al 2007, Cho et al 2014, Figure 1). These devices use pressure to hold the animals and allow for fluorescent imaging (Figure 2). The chips were designed in AutoCAD (Autodesk). Previously published protocols were used to make the PDMS replicas. Devices were controlled using an external valve system to regulate pressure in these channels. External components were built according to published protocols to automate the valve system (Rafael Gomez-Sjoberg, Microfluidics Lab, Lawrence Berkeley National Laboratory). Animals were imaged on a Zeiss 710 or Zeiss Axioscope inverted microscope. GCamP3 signals was used to confirm the function of the sensory neurons and prab-3 driven mcherry was used to visualize vesicles in axons.

Results : Animals were successfully immobilized and intermittently imaged up to 6 hours in tapered microfluidic devices (n=15). All animal survived and there was no significant change in the function of the sensory neurons following immobilization at 5 psi in the tapered channels. Pressures of 20psi were tested in these devices without malfunction of the devices. Vesicular markers were visualized these devices, which is promising for the further characterization of dynamics of axonal transport in the model.

Conclusions : Glaucoma is associated with high intraocular pressures and characterized by accelerated loss of retinal ganglion cells and their axons. Impaired axonal transport has been implicated as a pathogenic mechanism in glaucoma and impaired axonal transport along retinal ganglion cells has been demonstrated in animal and human glaucoma studies (Knox et. Al 2007). Here we show that external pressure can be modulated in these devices while allowing for simultaneous neuronal imaging. *Caenorhabditis elegans* provides a tractable nervous system with accessible genetic tools that can be used to study real-time neuronal and axonal response to direct pressure modulation.

This is an abstract that was submitted for the 2018 ARVO Annual Meeting, held in Honolulu, Hawaii, April 29 - May 3, 2018.

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